

Page 52, lines 20 and 21, **delete** the following (again added by the September 30, 1992 Preliminary Amendment):

"The publications cited in the aforementioned U.S. Patent No. 4,711,955 are also herein incorporated and made part of this disclosure."

and **replace** with the following:

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-- The publications cited in the aforementioned U.S. Patent Nos. 4,711,955, 5,328,824 and 5,449,767 are also herein incorporated and made part of this disclosure. --

Page 103, 10th line from the bottom of the page, after "of" and before "cytokines or cytokinins," change "Imphokines" to -- lymphokines -- .

**In The Claims:**

Cancel claims 240-282.

Add new claims 284-328 as follows:

-- 284. (New) A process for detecting a nucleic acid of interest in a sample, which process comprises the steps of:

6-14  
8-1  
hybridizing  
(a) ~~permitting hybridization of~~ said nucleic acid of interest in the sample with an oligo- or polynucleotide comprising at least one nucleotide selected from the group consisting of:

(i) a nucleotide having the formula



wherein

PM is a phosphate moiety,

SM is a sugar moiety,

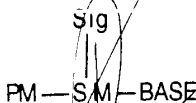
Enz-5(D8)(C2)

BASE is a pyrimidine, purine or 7-deazapurine, and

Sig is a detectable moiety,

wherein PM is attached at the 3' or the 5' position of the sugar moiety SM when said nucleotide is a deoxyribonucleotide and at the 2', 3' or 5' position when said nucleotide is a ribonucleotide, BASE is attached to the 1' position of SM from the N<sup>1</sup> position when BASE is a pyrimidine or the N<sup>9</sup> position when BASE is a purine or a 7-deazapurine, and Sig is covalently attached to BASE at a position other than the C<sup>5</sup> position when BASE is a pyrimidine, at a position other than the C<sup>8</sup> position when BASE is a purine and at a position other than the C<sup>7</sup> position when BASE is a 7-deazapurine;

(ii) a nucleotide having the formula



wherein

PM is a phosphate moiety,

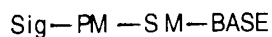
SM is a sugar moiety,

BASE is a pyrimidine, purine or 7-deazapurine, and

Sig is a detectable moiety,

wherein PM is a phosphate moiety, SM is a ribose or a deoxyribose sugar moiety, and BASE is a pyrimidine, purine or 7-deazapurine moiety, said PM being attached to SM at a position independently selected from the 2', 3', and 5' positions of SM when said nucleotide is a ribonucleotide, and at a position independently selected from the 3' and 5' positions when said nucleotide is a deoxyribonucleotide, said BASE being attached to the 1' position of SM from the N<sup>1</sup> position when BASE is a pyrimidine or the N<sup>9</sup> position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group; and

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(iii) a nucleotide having the formula



wherein

PM is a phosphate moiety,

SM is a sugar moiety,

BASE is a pyrimidine, purine or 7-deazapurine, and

Sig is a detectable moiety,

wherein PM is attached to the 3' or the 5' position of SM when said nucleotide is a deoxyribonucleotide and at the 2', 3' or 5' position when said nucleotide is a ribonucleotide, BASE is attached to the 1' position of SM from the N<sup>1</sup> position when BASE is a pyrimidine or the N<sup>9</sup> position when BASE is a purine, and Sig is covalently attached to PM; and

*Sig in said detectable Sig moieties in*

(b) detecting the presence of any of the oligo- or polynucleotides which have hybridized to said nucleic acid of interest. --

-- 285. (New) The process according to claim 284, wherein Sig comprises at least three carbon atoms. --

-- 286. (New) The process according to claim 284, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide. --

-- 287. (New) The process according to claim 284, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a radioactive component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

Enz-5(D8)(C2)

-- 288. (New) The process according to claim 287, wherein Sig comprises an electron dense component. --

289. (New) The process according to claim 288 wherein said electron dense component comprises ferritin. --

24  
-- 290. (New) The process according to claim 287, wherein Sig comprises a magnetic component. --

-- 291. (New) The process according to claim 290, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --

-- 292. (New) The process according to claim 291, wherein said magnetic component comprises magnetic beads. --

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G' 293. (New) The process according to claim 284, wherein Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar or a polysaccharide binding protein. --

-- 294. (New) The process according to claim 293, wherein the binding protein comprises a lectin. --

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G' 295. (New) The process according to claim 294, wherein the lectin comprises Concanavalin A. --

-- 296. (New) The process according to claim 294, wherein the lectin is conjugated to ferritin. --

-- 297. (New) The process according to claim 287, wherein Sig comprises an enzyme. --

-- 298. (New) The process according to claim 297, wherein the enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase,  $\beta$ -galactosidase, ribonuclease, glucose oxidase and peroxidase, or a combination thereof. --

-- 299. (New) The process according to claim 287, wherein Sig comprises a hormone. --

14  
-- 300. (New) The process according to claim 287, wherein Sig comprises a radioactive isotope. --

-- 301. (New) The process according to claim 287, wherein Sig comprises a metal-containing component. --

-- 302. (New) The process according to claim 301, wherein said metal-containing component is catalytic. --

-- 303. (New) The process according to claim 287, wherein Sig comprises a fluorescent component. --

-- 304. (New) The process according to claim 303, wherein the fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --

-- 305. (New) The process according to claim 287, wherein Sig comprises a chemiluminescent component. --

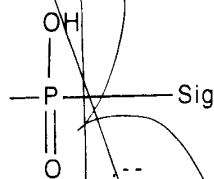
-- 306. (New) The process according to claim 287, wherein Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component. --

-- 307. (New) The process according to claim 284, wherein Sig is detectable when the oligo- or polynucleotide is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex. --

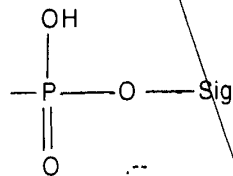
-- 308. (New) The process according to claims 284 or 307, wherein Sig is detectable when it is attached to the nucleotide directly or through a linkage group. --

34 -- 309. (New) The process according to claim 308, wherein said linkage group does not interfere substantially with the characteristic ability of Sig to form a detectable signal. --

-- 310. (New) The process according to claim 284, wherein Sig in said nucleotide (iii) is covalently attached to PM via the chemical linkage



-- 311. (New) The process according to claim 310, wherein said chemical linkage comprises



-- 312. (New) The process according to claim 284, wherein the oligo- or polynucleotide is terminally ligated or attached to a polypeptide. --

-- 313. (New) The process according to claim 284, further comprising contacting the sample with a polypeptide capable of forming a complex with Sig and a moiety which can be detected when the complex is formed. --

-- 314. (New) The process according to claim 313, wherein the polypeptide comprises a polylysine. --

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-- 315. (New) The process according to claim 314, wherein the polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin. --

-- 316. (New) The process according to claim 313, wherein Sig comprises a ligand and the polypeptide comprises an antibody thereto. --

-- 317. (New) The process according to claim 313, wherein the moiety which can be detected when the complex is formed is selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a radioactive component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

-- 318. (New) The process according to claim 284, wherein the nucleic acid of interest is derived from a living organism. --

-- 319. (New) The process according to claim 318, wherein the living organism is selected from the group consisting of prokaryotes and eukaryotes. --

-- 320. (New) The process according to claim 284, wherein the sample is suspected of containing an etiological agent and the nucleic acid of interest is naturally associated with the etiological agent. --

--321. (New) The process according to claim 320, wherein the sample is of human or animal origin and the etiological agent is selected from the group consisting of bacteria, virus and fungi. --

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-- 322. (New) The process according to claim 284, wherein the sample comprises a bacterium suspected of containing a nucleic acid of interest which imparts resistance to an antibiotic and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the sequence of the bacterium which confers resistance to the antibiotic. --

-- 323. (New). The process according to claim 322, wherein when said bacterium is *Streptococcus pyrogenes* or *Neisseria meningitidis*, said antibiotic is penicillin, wherein when said bacterium is *Staphylococcus aureus*, *Candida albicans*, *Pseudomonas aeruginosa*, *Streptococcus pyrogenes*, or *Neisseria gonorrhoea*, said antibiotic is a tetracycline, and wherein when said bacterium is *Mycobacterium tuberculosis*, said antibiotic is an aminoglycoside. --

-- 324. (New) The process according to claim 284, wherein the sample is suspected of containing a nucleic acid of interest associated with a genetic disorder and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid associated with the genetic disorder. --

-- 325. (New) The process according to claim 284, wherein the sample is suspected of containing a nucleic acid of interest associated with thalassemia and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid which is absent in the thalassemic subjects. --

-- 326. (New) The process according to claim 284, wherein said process is utilized for chromosomal karyotyping which comprises contacting the sample with a series of the oligo- or polynucleotides which are complementary to a series of known genetic sequences located on chromosomes. --

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-- 327. (New) The process according to claim 284, wherein the sample is suspected of containing a nucleic acid which includes a terminal polynucleotide sequence poly A and wherein the oligo- or polynucleotide comprises a modified poly U molecule in which at least one uracil moiety has been modified by chemical addition at the 5' position of Sig. --

-- 328. (New) The process according to claim 284, wherein said process is utilized to determine the number of copies of an individual chromosome in a sample. --

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In The Abstract of the Disclosure:

Delete the Abstract submitted with Applicants' September 30, 1992 Preliminary Amendment, and replace with the new substitute Abstract attached hereto Exhibit A.

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